Hepatitis C

1. DISEASE REPORTING

A. Purpose of Reporting and Surveillance

- 1. To identify sources of infection and to prevent further transmission from such sources.
- 2. To educate cases and contacts about transmission of hepatitis C virus and how to reduce the risk of transmission.
- 3. To better understand the epidemiology of hepatitis C virus infection and the burden of morbidity from chronic infection.

B. Legal Reporting Requirements (Acute and Chronic [initial diagnosis only])

- 1. Health care providers: notifiable to local health jurisdiction within one month
- 2. Hospitals: notifiable to local health jurisdiction within one month
- 3. Laboratories: detection of viral antigen, antibody or nucleic acid notifiable on a monthly basis
- 4. Local health jurisdictions: acute cases notifiable to the Washington State Department of Health (DOH) Communicable Disease Epidemiology Section (CDES) within 7 days of case investigation completion or summary information required within 21 days, chronic cases (initial diagnosis only) notifiable to DOH Infectious Disease and Reproductive Health (IDRH) within 7 days of case investigation completion or summary information required within 21 days

C. Local Health Jurisdiction Investigation Responsibilities

- 1. Determine if patients reported by health care providers and infection control staff meet the acute hepatitis C case definition or are newly diagnosed.
- 2. Begin follow-up investigation for acute hepatitis C within three work days.
 - a. Attempt to determine the source of infection.
 - b. Educate the case about hepatitis C and how to reduce the risk of transmission.
 - c. Educate the case about minimizing disease progression, focusing on the importance of vaccination for hepatitis A and hepatitis B and the need to avoid alcohol.
 - d. Report all *confirmed* acute hepatitis C cases (see definitions below) to CDES. Complete the acute hepatitis C report form (http://www.doh.wa.gov/notify/forms/hepc.doc) and enter the data into the Public Health Issues Management System (PHIMS) as an acute hepatitis C case.
- 3. Report all cases that meet the *confirmed* and *probable* hepatitis C, past or present case definitions (see definitions below reported in Washington as chronic hepatitis C) to DOH Infectious Disease and Reproductive Health. Complete as much of the chronic hepatitis C report form as is possible (http://www.doh.wa.gov/notify/forms/hepbcchronic.pdf) and enter the data into the Public Health Issues Management System (PHIMS) as a chronic hepatitis C case.

2. THE DISEASE AND ITS EPIDEMIOLOGY

A. Etiologic Agent

Hepatitis C virus is an RNA virus in the Flavivirus family. There are at least 6 hepatitis C virus genotypes: genotype 1 is the most common genotype in the United States and is associated with a lower rate of response to treatment. Concurrent infections with more than one genotype are possible. Hepatitis C virus is completely unrelated to the viruses that cause hepatitis A, B, D, and E.

B. Clinical Manifestations

Most persons with newly acquired infections are either asymptomatic or experience mild symptoms unlikely to prompt a visit to a health care provider. Approximately 20–30% of persons newly infected experience fatigue, abdominal pain, poor appetite or jaundice. Additional symptoms can include fever, dark urine, clay colored stool, nausea, vomiting, and joint pain. This clinical presentation is indistinguishable from other liver infections such as hepatitis A and hepatitis B. Fulminant hepatitis C infection is rare, but can be fatal. The most characteristic feature of acute hepatitis C is an elevation in serum alanine aminotransferase (ALT) levels. ALT levels fluctuate in persons with chronic hepatitis C.

Between 75% and 85% of infected individuals develop chronic infection. Long term complications of chronic infection can include chronic liver disease, cirrhosis and hepatocellular carcinoma. The risk of these sequelae increases for patients chronically infected with both hepatitis B virus and hepatitis C virus. Patients with signs of chronic liver disease due to hepatitis C virus are also at an increased risk of fulminant hepatic failure should they acquire hepatitis A virus infection.

C. Hepatitis C in Washington

In Washington, fewer than 30 acute hepatitis C cases are reported annually, reflecting low identification of acute infections. DOH receives over 5000 chronic hepatitis C reports each year.

D. Reservoir

Human beings with acute or chronic infections. While relatively few infected persons develop chronic infections, they are probably the most important sources of hepatitis C virus transmission because they are infectious for many years, compared to the few weeks that people with resolved acute hepatitis C are infectious.

E. Modes of Transmission (http://www.cdc.gov/hepatitis/HCV/HCVfaq.htm#section1)

Hepatitis C virus is transmitted primarily through large or repeated percutaneous (i.e., passage through the skin) exposures to infectious blood, such as

- Injection drug use (currently the most common means of HCV transmission in the United States)
- Receipt of donated blood, blood products, and organs (once a common means of transmission but now rare in the United States since blood screening became available in 1992)
- Needlestick injuries in healthcare settings
- Birth to an HCV-infected mother

HCV can also be spread infrequently through

- Sex with an HCV-infected person (an inefficient means of transmission)
- Sharing personal items contaminated with infectious blood, such as razors or toothbrushes (also inefficient vectors of transmission)
- Inappropriate infection control during surgery or other invasive healthcare procedures, such as injections (usually recognized in the context of outbreaks)

F. Incubation Period

For the ~20% of newly infected persons who develop symptoms of acute hepatitis C, the time period from exposure to onset of symptoms is generally 4–12 weeks with a range of 2 weeks to 6 months.

G. Period of Communicability

Communicability begins one or more weeks before onset of symptoms and persists in most persons indefinitely. It is not clear if communicability waxes and wanes, and if so, under what circumstances.

H. Treatment

Combination antiviral therapy with pegylated interferon (compared to regular interferon, "pegylated" interferon has a longer half-life, so the patient has therapeutic levels in the bloodstream for a longer time after a dose) and ribavirin results in a sustained viral response (absence of HCV RNA 6 months or more after treatment) in approximately 40–80% of patients with chronic hepatitis C. This varies by genotype, with lower response rates (up to 50%) in genotype 1, and higher response rates (up to 80%) in genotypes 2 and 3; most infections in the U.S. are genotype 1, unfortunately.

For additional information regarding treatment, see: http://www.cdc.gov/hepatitis/HCV/HCVfaq.htm

3. CASE DEFINITIONS

A. Hepatitis C, Acute (2007)

1. Clinical case definition

An acute illness with a discrete onset of any sign or symptom consistent with acute viral hepatitis (e.g., anorexia, abdominal discomfort, nausea, vomiting), **and** either a) jaundice, or b) serum alanine aminotransferase (ALT) levels >400 IU/L.

2. Laboratory criteria for diagnosis

One or more of the following three criteria:

- Antibodies to hepatitis C virus (anti-HCV) screening-test-positive with a signal to cut-off ratio predictive of a true positive as determined for the particular assay as defined by CDC. (URL for the signal to cut-off ratios: http://www.cdc.gov/hepatitis/HCV/LabTesting.htm), **OR**
- Hepatitis C virus recombinant immunoblot assay (HCV RIBA) positive, **OR**
- Nucleic acid test (NAT) for HCV RNA positive

Last Revised: December 2008 Page 3 of 12

AND, meets the following two criteria:

- IgM antibody to hepatitis A virus (IgM anti-HAV) negative, AND
- IgM antibody to hepatitis B core antigen (IgM anti-HBc) negative

3. Case classification

Confirmed: a case that meets the clinical case definition, is laboratory confirmed, and is not known to have chronic hepatitis C.

B. Hepatitis C, Past or Present (2005) [Reported in Washington as chronic hepatitis C]

1. Clinical description

Most HCV-infected persons are asymptomatic. However, many have chronic liver disease, which can range from mild to severe including cirrhosis and liver cancer.

- 2. Laboratory criteria for diagnosis
 - Anti-HCV positive (repeat reactive) by EIA, verified by an additional more specific assay (e.g. RIBA for anti-HCV or nucleic acid testing for HCV RNA), **OR**
 - HCV RIBA positive, OR
 - Nucleic acid test for HCV RNA positive, **OR**
 - Report of HCV genotype, **OR**
 - Anti-HCV screening-test-positive with a signal to cut-off ratio predictive of a true positive as determined for the particular assay (e.g., ≥3.8 for the enzyme immunoassays) as determined and posted by CDC.

3. Case classification

Probable: a case that is anti-HCV positive (repeat reactive) by EIA and has alanine aminotranferase (ALT or SGPT) values above the upper limit of normal, but the anti-HCV EIA result has not been verified by an additional more specific assay or the signal to cutoff ratio is unknown.

Confirmed: a case that is laboratory confirmed and that does not meet the case definition for acute hepatitis C.

4. DIAGNOSIS AND LABORATORY SERVICES

A. Laboratory Diagnosis

Two types of tests are used to diagnose hepatitis C virus infection; immunoglobulin (Ig) G antibody assays for anti-HCV (e.g., EIA, CIA, RIBA) and nucleic acid amplification tests (i.e., PCR). Anti-HCV generally can be detected 4–10 weeks after infection, but detection may be delayed up to 6 months or may never be detected in immunocompromised patients.

Anti-HCV Enzyme Immunoassays (**EIA**): Anti-HCV EIAs are highly sensitive tests generally used for screening purposes. This test indicates the presence of antibody only and cannot be used to distinguish between recent and past infection. Additional testing is required to determine if the individual is chronically infected. When the prevalence of

hepatitis C in a population decreases, the positive predictive value of the test will decrease (i.e., more false positive results will occur).

The <u>signal-to-cut-off ratio</u> can help to determine the likelihood that a positive anti-HCV EIA result represents a true positive. Signal-to-cut-off ratios are calculated by dividing the optical density (OD) value of the sample being tested (i.e., the client's test result) by the OD value of the assay cut-off for that run. Each test kit or assay has a signal-to-cut-off ratio above which the client has a 95% probability of being HCV-positive regardless of the prevalence of HCV in the population being tested.

For additional information regarding signal-to-cut-off ratios and signal-to-cut-off ratios predictive of a true positive ≥ 95% of the time, see: http://www.cdc.gov/hepatitis/HCV/LabTesting.htm

Recombinant immunoblot assay (RIBA): RIBA is a more *specific* test for anti-HCV antibody (i.e., the test is good for ruling out false positives). It is not as *sensitive* as the anti-HCV EIA and should not be used as an initial screening test, but it is useful for ruling out false-positive EIA tests.

Qualitative and qualitative tests to detect viral nucleic acids (HCV RNA PCR):

Polymerase chain reaction (PCR) is used to measure HCV RNA and indicates active replication of the virus (e.g., the chronic carrier state). The qualitative PCR is more sensitive than the quantitative assay and is preferred for the initial test. The quantitative PCR is often used to guide initial treatment decisions and to follow the progress of individuals undergoing treatment.

For information regarding interpreting laboratory tests for hepatitis C, see: http://www.cdc.gov/hepatitis/HCV/PDFs/hcv_graph.pdf

See Appendix A for a glossary of hepatitis test terms.

B. Tests Available at the Washington State Public Health Laboratories (PHL)

PHL does not perform serologic or nucleic acid tests for hepatitis C, but these tests are widely available at commercial laboratories. In certain circumstances, CDES may request a specimen from a case for molecular sequencing at the Centers for Disease Control and Prevention.

C. Specimen Collection

Serum can be collected from patients from the onset of symptoms.

5. ROUTINE CASE INVESTIGATION

A. Evaluate the Diagnosis

- 1. Health Care Provider and Infection Control Staff Reports:
 - Check PHIMS and/or your other local hepatitis C registry to determine if the patient was previously reported as either acute or chronic hepatitis C.
 - Obtain information from the health care provider, hospital infection control staff, or patient to determine if the patient meets the acute hepatitis C case definition.

Last Revised: December 2008 Page 5 of 12

- If the patient has symptoms consistent with acute hepatitis, determine if hepatitis A and hepatitis B have been ruled out since these infections are clinically indistinguishable from hepatitis C.
- If the patient meets the acute hepatitis C case definition, proceed to Section 5B.
- Local health jurisdictions are encouraged to provide education (see Section 6) to patients who meet the hepatitis C, past or present case definition, focusing efforts on those likely to have a new diagnosis.

2. <u>Laboratory Reports Only (including reports from hospital laboratories)</u>:

- Check PHIMS and/or your other local hepatitis C registry to determine if the patient was previously reported as either acute or chronic hepatitis C.
- If the patient was not previously reported, complete as much of the chronic hepatitis
 C form as is possible and enter the information into PHIMS as a chronic hepatitis C
 case.
- Resource permitting, local health jurisdictions are encouraged to contact the provider or laboratory to determine if the patient meets the acute hepatitis C case definition and/or is newly diagnosed. Persons who meet the acute hepatitis C case definition should be investigated as described below. Local health jurisdictions can consider faxing the hepatitis C data collection form (Appendix B) to the provider to assist with data collection.
- Resource permitting, local health jurisdictions are encouraged to provide education (see Section 6) to persons who meet the hepatitis C, past or present case definition, focusing efforts on those likely to have a new diagnosis.

B. Identify the Source of Infection

For persons with acute hepatitis C and those suspected to have been infected through medical or commercial procedures, ask about potential exposures during the 6 months prior to onset including:

- Parenteral drug use.
- Occupational or other needlestick injuries.
- Blood transfusion or receipt of immunoglobulins or other blood products.
- Potential medical or dental exposures within the 6 months prior to onset of current illness, including organ or tissue transplant, dialysis, dental or surgical care.
- Other parenteral exposures within the 6 months prior to onset of current illness, including tattooing, piercing, or acupuncture.
- High-risk sexual contact (multiple partners, history of other STDs, anal sex, etc.)

C. Identify Contacts

1. Determine if case has donated blood or plasma in the 6 months prior to onset or any time thereafter. If so, notify the relevant blood bank or plasma center with particulars (date, etc.)

2. Identify sexual or needle-sharing contacts and others who have had direct (percutaneous or mucosal) exposure to blood.

D. Environmental Evaluation

Usually none, unless transmission occurs in a dialysis center or health care facility.

6. CONTROLLING FURTHER SPREAD:

A. Infection Control Recommendations / Case Management

- 1. Hospitalized patients should be cared for using standard precautions. All health care providers with risk for blood exposure should complete the hepatitis B vaccine series to prevent dual infections.
- 2. <u>Work or Child Care Restrictions</u>: No occupational, school, or child care restrictions are necessary for hepatitis C virus (HCV)-infected individuals.
- 3. The case should be instructed that their blood and other secretions (particularly semen and vaginal secretions) are infectious to others. They should be educated about ways to reduce the spread of their infection to others.
 - Cases should not share items potentially contaminated with blood (e.g., needles, syringes, razors, toothbrushes).
 - Infected persons should not share hypodermic needles, syringes, or drug works with
 other people. Disposable needles should be used only once. As a last resort,
 undiluted household bleach can be used to clean syringes and needles. Active
 injection drug users should be directed to needle exchange programs and drug
 rehabilitation services.
 - Cuts and skin lesions should be kept covered.
 - Cases should understand the risk of sexual transmission is low but not absent. Hepatitis C virus-positive persons with one long-term steady sex partner should discuss the risk of transmission with their partner. Hepatitis C virus-positive persons engaged in high-risk sexual activities should be counseled to use latex barriers correctly every time they have sex.
 - Infected persons should not donate blood, plasma, tissues, organs or semen.
 - HCV RNA-positive persons who seek medical or dental care should notify involved personnel of their hepatitis C status.
- 4. Persons with acute hepatitis C should have a repeat test for HCV RNA six months after the first to determine the clearance or continued presence of viremia. Those who continue to be HCV RNA-positive are considered confirmed chronic infections, and should be counseled accordingly.
- 5. Persons with chronic hepatitis C should be educated to protect their liver from further harm. The case should:
 - See a provider with experience managing chronic hepatitis C.
 - Ask their provider about use of over-the-counter drugs (e.g., acetaminophen) that can damage the liver.

Last Revised: December 2008 Page 7 of 12

- Stop behaviors that could result in transmission of hepatitis C virus.
- Not drink alcohol.
- Get vaccinated against hepatitis A and B if susceptible.

B. Contact Management

1. Passive Immunization

Passive immunization with immune globulin is *not* effective against HCV.

2. Education

- Long term sexual contacts and persons who have had direct (percutaneous or mucosal) exposure to blood (e.g., needle-sharing partners) should be educated about transmission of hepatitis C and tested for HCV. Routine screening is not recommended for household (nonsexual) contacts of HCV-positive patients.
- Active injection drug users should be directed to needle exchange programs and drug rehabilitation services.

3. Active Immunization

There is no vaccine. Contacts who are susceptible and at risk for hepatitis A and hepatitis B should be vaccinated against these viruses to prevent dual infections.

C. Environmental Measures

Ensure that surfaces and objects contaminated with blood are properly disinfected using gloves and appropriate disinfectant solutions.

7. MANAGING SPECIAL SITUATIONS

A. Needlesticks and Similar Exposures

The risk of hepatitis C virus (HCV) transmission following unintentional parenteral exposure is real (approximately 2%) but there is no preventive therapy. Current CDC guidelines recommend a hepatitis C virus antibody test and ALT level at baseline and at 6 months to capture the full seroconversion time-window. PCR testing for HCV may be performed at 4–6 weeks. Risk for HIV and hepatitis B virus should also be assessed using current CDC guidelines.

Centers for Disease Control and Prevention. Updated U.S. Public Health Service guidelines for the management of occupational exposures to HBV, HCV, and HIV and recommendations for postexposure prophylaxis. MMWR 2001;50(RR-11):1–52. Available on the web at: http://www.cdc.gov/mmwr/PDF/RR/RR5011.pdf

B. Case Is a Recent Blood Donor or Recipient

The blood bank should be notified so that any unused product can be recalled.

C. Case Is Pregnant

Inform the woman that the transmission risk with pregnancy is about 5%.

Last Revised: December 2008

D. Case is a Suspected Introgenic Infection

If a case underwent a medical or dental procedure and has no other identified plausible source of infection, contact the provider and review infection control procedures. Consider storing a blood specimen (if available) for genotyping in the event an additional case is identified with a potential shared exposure.

If two or more iatrogenic cases occur in patients of the same dental or health care provider, and the cases have no other identified plausible source of infection, or other circumstances suggesting the possibility of iatrogenic infection, notify Communicable Disease Epidemiology Section.

8. ROUTINE PREVENTION

A. Immunization Recommendations

There is currently no vaccine available for hepatitis C virus (HCV).

B. Routine Prevention (Source: http://www.cdc.gov/ncidod/diseases/hepatitis/c/fact.htm)

Provide the following information to persons at risk of infection:

- There is no vaccine to prevent hepatitis C.
- Do not shoot drugs; if you shoot drugs, stop and get into a treatment program; if you can't stop, never share needles, syringes, water, cleaning material, or "works", and get vaccinated against hepatitis A and B.
- Do not share personal care items that might have blood on them (razors, toothbrushes).
- If you are a health care or public safety worker, always follow routine barrier precautions and safely handle needles and other sharps; if susceptible, get vaccinated against hepatitis B.
- Consider the risks if you are thinking about getting a tattoo or body piercing. You might get infected if the tools have someone else's blood on them or if the artist or piercer does not follow good infection control practices.
- HCV can be spread by sex, but this is rare. If you are having sex with more than one steady sex partner, use latex barriers correctly and every time to prevent the spread of sexually transmitted diseases. You should also get vaccinated against hepatitis A and B, if susceptible.
- If you are HCV positive, do not donate blood, organs, or tissue.

ACKNOWLEDGEMENTS

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Last Revised: December 2008 Page 9 of 12

Appendix A: GLOSSARY OF TERMS

ALT/AST: these are both liver enzymes classified as serum aminotransferases or transaminases and are useful indicators of liver damage. Alanine aminotransferase is usually abbreviated as ALT (or SGOT) and is particularly sensitive for assessing liver damage secondary to HCV. Aspartate aminotransferase is referred to as AST (or SGPT). In acute hepatitis A or B, an elevation in either one is required to meet the case definition, while the hepatitis C case definition requires an elevation in the ALT to over 400 IU/L.

Hepatitis A Testing

IgM anti-HAV: IgM antibody to HAV. Indicates acute infection with HAV.

Anti-HAV total: combined antibody to HAV including IgM with acute infection and IgG with long term protection.

Hepatitis B Testing

HBsAg: hepatitis B surface antigen, a marker of replicating virus. It occurs as part of acute infection and persists in chronic infection. Its presence indicates that the patient is considered to be infectious.

Anti-HBs: hepatitis B surface antibody. It demonstrates immunity through infection or vaccination.

IgM Anti-HBc: IgM antibody to hepatitis B core antigen, indicative of recent infection with hepatitis B virus. Antibody to core antigen only occurs following infection, not immunization.

Anti-HBc: total antibody to hepatitis B core antigen. This marker becomes positive at the onset of symptoms in acute hepatitis B then persists for life. Therefore, it does not distinguish between recent, past, or chronic infection.

HBeAg: hepatitis B e antigen, a core protein exported from infected liver cells and a marker of high levels of infectivity. Similar to HBsAg, it occurs (albeit transiently) as part of acute infection and may persist in chronic infections.

HBeAb: hepatitis B e antibody is produced by the immune system temporarily during acute HBV infection and may persist in chronic infections. Spontaneous conversion from e antigen to e antibody is a predictor of long-term clearance of HBV in patients undergoing antiviral therapy and indicates lower levels of HBV. Chronic hepatitis B surface antigen carriers can be positive for either HBeAg or anti-HBe, but are less infectious when anti-HBe is present.

Hepatitis B virus DNA: signifies active replication of the virus and indicates that the patient is infectious. It is usually measured to test for chronic infection, and the viral load may be used to decide whether treatment is warranted.

Hepatitis C

Anti-HCV EIA: enzyme immunoassay to measure HCV antibody. Indicates presence of antibody only and cannot be used to distinguish between recent and past infection. Additional testing is required to determine if the individual is chronically infected.

Signal-cutoff ratio: can be used to help determine the likelihood that a positive anti-HCV EIA represents a true positive. Each assay has a cut-off value that is considered a "positive" result; the signal-cutoff ratio can be calculated by dividing the optical density (OD) value of the sample being tested (e.g., the client's test result) by that particular assay's cut-off value. Each test kit or assay has a signal-cutoff ratio above which the client has a 95% probability of being HCV-positive and should be reported as a case.

RIBA: recombinant immunoblot assay, a more *specific* test for anti-HCV antibody (in other words, it's good for ruling out false positives). It is not as *sensitive* as the anti-HCV EIA and should not be used as an initial screening test, but it is useful for ruling out false-positive EIA tests.

PCR: polymerase chain reaction, used to measure HCV RNA and indicates active replication of the virus (e.g., the chronic carrier state). The qualitative PCR is more sensitive than the quantitative assay and is preferred for the initial test. The quantitative PCR is often used to guide initial treatment decisions and to follow the progress of individuals undergoing treatment.

HCV genotype: HCV can be divided into at least 6 different genotypes. Genotype 1 is the most common in the United States, accounting for 70–75% of infections. A positive genotype indicates the presence of HCV RNA.

Appendix B: SAMPLE HEPATITIS C DATA COLLECTION FORM

[Local health Jurisdiction Name]

[LHJ Address]

HEPATITIS C DATA COLLECTION

We have received a positive Hepatitis C laboratory report for the following patient. Please complete the demographic and risk information in the box below. This confidential information is required for completion of the mandatory case report. Fax the completed form to [fax number]. If you have any questions please call [LHJ investigator].

questions p	lease call [LHJ investigator].	
CLIENT		BIRTHDATE/ LAB REPORT DATE//
ADDRESS		PROVIDER
-		_
ETHNICITY		GENDER
Hispanic	☐ Non Hispanic	☐ Male ☐ Female
RACE Amer Indian	n/Alaska Native	Native HI/Other PI ☐ Black ☐ African Amer ☐ White ☐ Other
CLINICAL		
When was the patient first diagnosed with hepatitis C?/ Why was the patient recently tested for hepatitis C? Y N DK NA Did the patient experience a discrete onset of symptoms? If yes, onset/ Is the patient jaundiced?		
LABORATORY (P=positive, N=negative, I=indeterminate, O=other, NT=not tested) P N I O NT		
LIFETIME EXPOSURE HISTORY (Please complete as much as possible.) Y N DK NA		
☐ ☐ ☐ ☐ Contact with a confirmed or suspect hepatitis C case If yes, type of contact: ☐ Household ☐ Sexual ☐ Needle share ☐ Birth mother ☐ Other:		
Factor concentrates before 1987 Blood products or solid organ transplant (If yes, date of receipt://) Employed in job with potential for exposure to human blood or body fluids Injection street drug use Chronic hemodialysis		